REMARKS

Claims 1-33 are pending in the application. Claims 1-20 have been cancelled. New claims 21-33 have been added. These amendments are supported at page 2, paragraph 25, page 2, paragraph 38 and page 3, paragraphs 43 and 48-49.

BACKGROUND

ABP-1 (angiostatin binding protein-1, SEQ ID NO: 2) is a protein with a region (Big-3, shown in SEQ ID NO: 4) that has the ability to bind a fragment of plasminogen such as the first four Kringle domains. Such a fragment of plasminogen is called angiostatin and it exhibits activity against angiogenesis. Experiments have demonstrated that ABP-1 plays a role in mediating angiostatin's signaling pathways, and consequently its anti-angiogenic activity, by acting as a receptor to angiostatin.

Having identified ABP-1, the invention encompasses variants of ABP-1 and its homologs and fragments that have the same angiostatin-binding activity as ABP-1. Such variants, homologs and fragments are readily identifiable according to conventional methods of protein synthesis and assays, coupled with the working examples disclosed in the specification, as discussed in detail below.

The invention further encompasses antibodies to ABP-1, which can also be identified and assayed according to conventional methods and assays, coupled with the working examples disclosed in the specification. Such antibodies are useful, for example, in immunoassays and medicaments.

Restriction

Applicants acknowledge the Examiner's withdrawal of the restriction requirement between groups I and II of the claimed invention and the new restriction requirement between claims 1-19 (antibody products) and claim 20 (method of treatment). Claims 1-20 have been cancelled and new claims 21-33 have been added. Claims 21-32 cover antibody products and claim 33 covers a method of treatment.

Applicants respectfully submit that examining the antibody product and method of treatment claims do not present an undue burden for the Examiner, particularly because

claim 33 is a linking claim that incorporates the subject matter of the pending product claims by virtue of its dependency.

Applicants note that such restrictions were not applied during the parent case of the pending application, which issued as U.S. Patent No. 6,908,898. In that case, claims to (1) an isolated protein, (2) a composition, (3) a method of manufacturing and (4) a method of treatment all issued in the same patent. Applicants respectfully request that the Examiner reconsider the new restriction requirement, particularly in light of the parent case and claim 33's incorporation of the limitations of the examined claims by virtue of its dependency thereon.

Rejections under 35 U.S.C. § 101

The Examiner has rejected claims 1-19 as claiming an invention that is not directed to statutory subject matter. These claims have been cancelled. New claims 21-33 have been added and recite "isolated" antibodies. Thus, this rejection is moot.

Rejections under 35 U.S.C. § 112, ¶ 1 (Written Description)

The Examiner has rejected claims 1, 2, 6-8, 12-14, 18 and 19 as not being adequately described in the specification in such a way as to convey to one skilled in the art, at the time the application was filed, that Applicants had possession of the claimed invention. According to the Examiner, the Applicant has not presented sufficient written description to show that a peptide having at least 80% sequence identity to SEQ ID NOS: 2 and 4 or a peptide having at least 10 contiguous amino acid residues of SEQ ID NO: 2 would maintain the functional activity as recited in the claims. The Examiner also asserts that peptides encompassed by the phrase 80% sequence identity to SEQ ID NOS: 2 and 4 may not have the recited function (page 7 of the Office Action) and that SEQ ID NO: 4 would not have anti-angiogenic activity because it would not have an intracellular domain for signal transduction (page 13 of the Office Action).

Factors to be considered in determining whether there is sufficient written description include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function and methods of making the claimed

invention. Where the specification discloses relevant identifying characteristics, i.e., physical, chemical and/or functional characteristics, sufficient to allow a skilled artisan to recognize that the applicant was in possession of the claimed invention, a rejection for lack of written description under Section 112, first paragraph, cannot be maintained. *Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 323 F.3d 956 (Fed. Cir. 2002).

The presently pending claims encompass antibodies that bind proteins with 80% sequence homology or greater to SEQ ID NO: 4 and antibodies that bind proteins having SEQ ID NO: 4. Applicants maintain that the claims are supported at page 2, paragraph 25, which defines peptides that are substantially similar to SEQ ID NO: 4; page 2, paragraph 38 and page 3, paragraphs 48-49, which disclose that procedures for making protein variants are known in the art; and page 2, paragraph 26, which describe the conditions for hybridizing to a nucleotide sequence. Furthermore, the specification discloses working examples that describe an assay for assessing the function of the anti-angiogenic activity of a protein with 80% sequence homology or greater to SEQ ID NO: 4 (page 8, paragraph 131 – page 9, paragraph 144). The specification also sets forth the relationship between the structure of a protein with 80% sequence homology or greater to SEQ ID NO: 4 and its anti-angiogenic function because SEQ ID NO: 4 contains the angiostatin binding domain of the protein (page 5, paragraph 73 – page 6, paragraph 87).

Applicants further submit that the claimed antibodies are described in such a way as to convey to one skilled in the art that Applicants had possession of the claimed antibodies at the time of filing because the description of an antibody is implicit when the antigen (i.e., the protein having 80% sequence homology or greater to SEQ ID NO: 4) has been fully characterized. According to current law:

> [B]ased on our past precedent, as long as an applicant has disclosed a *"fully characterized"* antigen," either by its structure, formula, chemical name, or physical properties, or by depositing the protein in a public depository, the applicant can then claim an antibody by its binding affinity to that described antigen.

Noelle v. Lederman, 355 F.3d 1343, 1349 (Fed. Cir. 2004) (emphasis in original). The Written Description Guidelines also indicate that one of skill in the art would be able to identify antibodies that bind a fully characterized antigen because making antibodies is a mature technology: "A claim directed to 'any antibody which is capable of binding to

antigen X' would have sufficient support in a written description that disclosed '*fully characterized* antigens.' Written Description Guidelines at 60, available at http://www.uspto.gov/web/menu/written.pdf. Antibodies to SEQ ID NO: 4 have been actually reduced to practice, as described on page 8, paragraphs 128-130. Moreover, the antigen's nucleotide (SEQ ID NO: 1) and amino acid (SEQ ID NO: 2) sequences are disclosed. The antigen's function is also disclosed as a receptor of angiostatin (page 3, paragraph 40) that mediates angiogenesis (page 8, paragraph 141-143). Thus, the antigen is fully characterized in the specification.

Turning to the Examiner's concern that peptides with at least 80% sequence identity to SEQ ID NOS: 2 and 4 may not have the recited function (page 7 of the Office Action), Applicants submit that such peptides are not encompassed by the claims because the claims also recite that the protein has anti-angiogenic activity. As noted earlier, the specification teaches an assay for anti-angiogenic activity.

Turning to the Examiner's concern that SEQ ID NO: 4 would not have anti-angiogenic activity because it would not have an intracellular domain for signal transduction (page 13 of the Office Action). Applicants submit that SEQ ID NO: 4's anti-angiogenic activity arises from its association with the recited fragment of plasminogen. Thus, the protein having 80% sequence homology or greater to SEQ ID NO: 4 is encompassed by the claims because it binds the recited fragment of plasminogen regardless of the location of the signal transduction domain. *See* page 1, paragraph 8.

Applicants submit that, given the teachings of the specification of both structural and functional features of anti-angiogenic proteins encompassed by the claims, a sufficient written description has been provided. Therefore, the rejection is erroneous and Applicants respectfully request withdrawal of the rejections of these and all pending claims under 35 U.S.C. § 112, first paragraph.

Rejections under 35 U.S.C. § 112, ¶ 1 (Enablement)

The Examiner has rejected claims 1, 2, 6-8, 12-14, 18 and 19 as not enabling one skilled in the art to make and use the claimed invention according to 35 U.S.C. § 112, paragraph 1. The Examiner alleges that the specification, while being enabling for an antibody or antibody fragment that binds to a protein comprising an amino acid sequence

as set forth in SEQ ID NOS: 2, 3 or 4, is not enabling for a peptide having at least 80% sequence identify to SEQ ID NOS: 2 and 4 or a peptide having at least 10 contiguous amino acid residues of SEQ ID NO: 2.

The test for enablement is whether one reasonably skilled in the art could make or use the invention, without undue experimentation, from the disclosure in the patent coupled with information known in the art at the time the patent application was filed. *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988).

The presently pending claims encompass antibodies that bind proteins with 80% sequence homology or greater to SEQ ID NO: 4 and antibodies that bind proteins having SEQ ID NO: 4. Applicants submit that one skilled in the art would be able to make and use antibodies that bind such a peptide because making and identifying variant proteins to a given sequence is routine in the art. Applicants maintain that the specification describes procedures that are conventional in the art for making protein variants (*see* page 2, paragraph 38 and page 3, paragraphs 48-49). Applicants further submit that one of ordinary skill in the art would also be able to assess the activity of peptides having 80% sequence homology or greater to SEQ ID NO: 4 and their antibodies based on the disclosed assays (page 8, paragraph 131 – page 9, paragraph 144). Moreover, antibodies to SEQ ID NO: 4 have been actually reduced to practice, as described in the specification at page 8, paragraphs 128-130. Thus, undue experimentation would not be required by one of ordinary skill in the art to develop the antibodies encompassed by the claims.

Accordingly, Applicants respectfully submit that the pending claims satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph and request that this ground of rejection be withdrawn.

CONCLUSION

It is respectfully submitted that the present application is now in condition for allowance, which action is respectfully requested. The Examiner is invited to contact Applicants' representative to discuss any issue that would expedite allowance of the subject application.

Any fees for extension(s) of time or additional fees that are required in connection with the filing of this response are hereby petitioned under 37 C.F.R. § 1.136(a), and the Commissioner is authorized to charge any such required fees or to credit any overpayment to Kenyon & Kenyon LLP Deposit Account No. 11-0600.

Respectfully submitted,

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